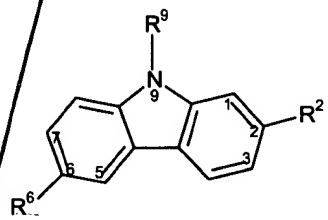
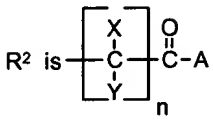
reducing or eliminating undesirable side effects associated with simultaneous inhibition of the activity of constitutive cyclo-oxygenase-1 (COX-1) by selectively inhibiting COX-2 activity with reference to COX-1 activity, wherein the selectivity ratio of COX-2:COX-1 activity inhibition is at least 3:1 based on *ex vivo* inhibition levels in whole blood measured at a dose giving ≥ 80% COX-2 inhibition, comprising administering to said member of the species *Canis familiaris* an amount therapeutically effective for treating pain and inflammation in accordance with the above-recited limitations, of an anti-inflammatory selective COX-2 inhibitory compound comprising a compound of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, with the proviso that said compound is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.

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4. (Twice Amended) A method for treating or preventing inflammatory processes and diseases as in Claim 1 further comprising wherein said inhibitory compound is used in combination with one or more other therapeutically active agents under the following conditions:

A. where a joint has become seriously inflamed as well as infected at the same time by bacteria, fungi, protozoa, and/or virus, said inhibitory compound is administered in combination with one or more antibiotic, antifungal, antiprotozoal, and/or antiviral therapeutic agents;

B. where a multi-fold treatment of pain and inflammation is desired, said inhibitory compound is administered in combination with inhibitors of other mediators of inflammation, comprising one or more members independently selected from the group consisting of:

1. NSAIDs;
2. H_1-receptor antagonists;
3. kinin-B_1 - and B_2 receptor antagonists;
4. prostaglandin inhibitors selected from the group consisting of PGD-, PGF-PGI_2 -, and PGE-receptor antagonists;
5. thromboxane A_2 (TXA2-) inhibitors;
6. 5- and 12-lipoxygenase inhibitors;
7. leukotriene LTC_4 - LTD_4/LTE_4- , and LTB_4 -inhibitors
8. PAF-receptor antagonists;
9. gold in the form of an aurothio group together with one or more hydrophilic groups;
10. immunosuppressive agents selected from the group consisting of cyclosporine, azathioprine, and methotrexate;
11. anti-inflammatory glucocorticoids;
12. penicillamine;
13. hydroxychloroquine;
14. anti-gout agents including colchicines; xanthine oxidase inhibitors including allopurinol; and uricosuric agents selected from probeneoid, sulfinpyrazone, and benzobromarone;

C. where older dogs are being treated for disease conditions, syndromes, and symptoms found in geriatric dogs, said inhibitory compound is administered in combination with one or more member independently selected from the group consisting of:

C2 cont

1. cognitive therapeutics to counteract memory loss and impairment;

2. anti-hypertensives and other cardiovascular drugs intended to offset the consequences of atherosclerosis, hypertension, myocardial ischemia, angina, congestive heart failure, and myocardial infarction, selected from the group consisting of:

a. diuretics;

b. vasodilators;

c. ß-adrenergic receptor antagonists;

d. angiotensin-II converting enzyme inhibitors (ACE-inhibitors), alone or optionally together with neutral endopeptidase inhibitors;

e. angiotensin II receptor antagonists;

f. renin inhibitors;

g. calcium channel blockers;

h. sympatholytic agents;

i. α_2-adrenergic agonists;

j. α-adernergic receptor antagonists; and

k. HMG-CoA-reductase inhibitors (anti-hypercholester-olemics);

3. antineoplastic agents selected from:

a. antimitotic drugs selected from:

i. vinca alkalodis selected from:

[1] vinblastine, and

[2] vincristine;

4. growth hormone secretagogues;

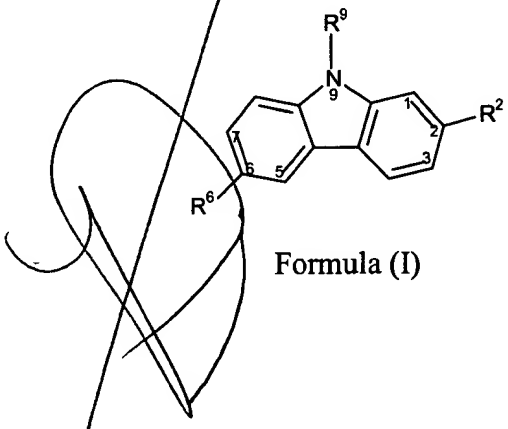
5. strong analgesics;

6. local and systemic anesthetics; and

7. H_2 -receptor antagonists, proton pump inhibitors, and other gastroprotective agents.

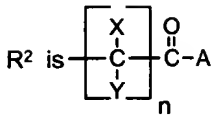
5. (Amended) A pharmaceutical composition for treating or preventing pain and inflammatory processes and diseases associated with the activity of inductible cyclo-oxygenase-2 (COX-2) in a member of the species *Canis familaris* in need of such treatment, while at the same time reducing or eliminating undesirable side effects associated with simultaneous inhibition of the activity of constitutive cyclo-oxygenase-1 (COX-1), comprising:

A. a therapeutically effective amount for treating pain and inflammation, of an anti-inflammatory selective COX-2 inhibitory compound which selectively inhibits COX-2 activity with reference to COX-1 activity, wherein the selectivity ration of COX-2; COX-1 activity inhibition is at least 3:1 based on *ex vivo* inhibition levels in whole blood measured at a dose giving ≥ 80% COX-2 inhibition, comprising an anti-inflammatory selective COX-2 inhibitory compound comprising a compound of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are

C3 cm therapeutically active for treating or preventing pain and inflammation, with the proviso that said compound is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.

C4 8. (Amended) A pharmaceutical composition as in Claim 5 further comprising wherein said anti-inflammatory selective COX-2 inhibitory compound is provided in a dosage form suitable for systemic administration by:

A. injection or infusion in suitable liquid form which is intraarterial, intra- or transdermal, subcutaneous, intramuscular, intraspinal, intrathecal, or intraveneous, wherein said inhibitory compound:

1. is contained in solution as a solute;

2. is contained in a discontinuous phase of an emulsion, or the discontinuous phase of an inverse emulsion which inverts upon injection or infusion, said emulsions containing suitable emulsifying agents; or

3. is contained in a suspension as a suspended solid in colloidal or microparticulate form, said suspension containing suitable suspending agents;

B. injection or infusion into suitable body tissues or cavities as a depot, wherein said composition provides storage of said inhibitor and thereafter delayed-, sustained- and/or controlled-release of said inhibitory compound for systemic distribution;

C. instillation, inhalation or insufflation into suitable body tissues or cavities in suitable solid form, where said inhibitory comound:

1. is contained in a solid implant composition providing delayed-, sustained-, and/or controlled-release of said inhibitory comound:

2. is contained in a particulate composition to be inhaled into the lungs; or

3. is contained in a particulate composition to be blown into said suitable body tissues or cavities, wherein said composition optionally provides delayed-, sustaine-, and/or controlled release of said inhibitory compound; or

D. ingestion is suitable solid or liquid form for peroral delivery of said inhibitory compound, where said inhibitory compound:

1. is contained in a solid dosage form; or

2. is contained in a liquid dosage form.

10. (Amended) A pharmaceutical composition as in Claim 9 comprising an oral controlled release dosage form able to maintain plasma levels of said pharmaceutical composition above approximately 10 μg/mL for a period of time greater than 10.5 hours, when administered at a dose of about 2 mg/lb or less.

11. (Twice Amended) A pharmaceutical composition as in Claim 5, further comprising said anti-inflammatory selective COX-2 inhibitory compound in combination with one or more other therapeutically active agents independently selected from the group consisting of:

A. anti-infectious agents comprising one or more antibiotic, antifungal, antiprotozoal, or antiviral therapeutic agents;

B. inhibitors of other mediators of inflammation, comprising one or more members independently selected from the group consisting of:

1. NSAIDs;

2. H_1-receptor antagonists;

3. kinin-B_1 - and B_2 receptor antagonists;

4. prostaglandin inhibitors selected from the group consisting of PGD-, PGF-PGI_2 -, and PGE-receptor antagonists;

5. thromboxane A_2 (TXA2-) inhibitors;

6. 5- and 12-lipoxygenase inhibitors;

7. leukotriene LTC_4 - LTD_4/LTE_4- , and LTB_4 -inhibitors

8. PAF-receptor antagonists;

9. gold in the form of an aurothio group together with one or more hydrophilic groups;

10. immunosuppressive agents selected from the group consisting of cyclosporine, azathioprine, and methotrexate;

11. anti-inflammatory glucocorticoids;

12. penicillamine;

13. hydroxychloroquine;

14. anti-gout agents including colchicines; xanthine oxidase inhibitors including allopurinol; and uricosuric agents selected from probeneoid, sulfinpyrazone, and benzobromarone;

C. where older dogs are being treated for disease conditions, syndromes, and symptoms found in geriatric dogs, said inhibitory compound is administered in combination with one or more member independently selected from the group consisting of:

1. cognitive therapeutics to counteract memory loss and impairment;

2. anti-hypertensives and other cardiovascular drugs intended to offset the consequences of atherosclerosis, hypertension, myocardial ischemia, angina, congestive heart failure, and myocardial infarction, selected from the group consisting of:

a. diuretics;

b. vasodilators;

c. ß-adrenergic receptor antagonists;

d. angiotensin-II converting enzyme inhibitors (ACE-inhibitors), alone or optionally together with neutral endopeptidase inhibitors;

e. angiotensin II receptor antagonists;

f. renin inhibitors;

g. calcium channel blockers;

h. sympatholytic agents;

i. α_2-adrenergic agonists;

j. α-adernergic receptor antagonists; and

k. HMG-CoA-reductase inhibitors (anti-hypercholester-olemics);

3. antineoplastic agents selected from:

a. antimitotic drugs selected from:

i. vinca alkalodis selected from:

[1] vinblastine, and

[2] vincristine;

4. growth hormone secretagogues;

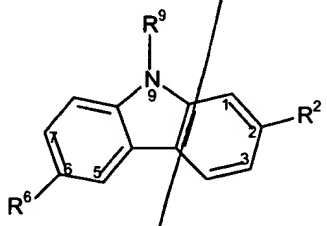
5. strong analgesics;

6. local and systemic anesthetics; and

7. H_2 -receptor antagonists, proton pump inhibitors, and other gastroprotective agents.

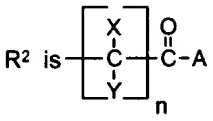
15. (Amended) A method of preventing or alleviating pain and inflammatory processes and diseases in a member of the species Canis familiaris with reduced or no

undesirable gastro-intestinal side effects normally associated with administration to said member of non-steroidal anti-inflammatory drugs, said member having been examined by a veterinarian practitioner and diagnosed as in need of such treatment using a drug which selectively inhibits inducible cyclo-oxygenase-2 (COX-2) to prevent or alleviate said pain and inflammatory processes with substantially no inhibition of constitutive cyclo-oxygenase-1 (COX-1) to reduce or avoid said side effects, which comprises administering to said member of the species Canis familiaris that has been so examined and diagnosed an amount therapeutically effective to treat or prevent pain and inflammation with reduction in or avoidance of said side effects of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

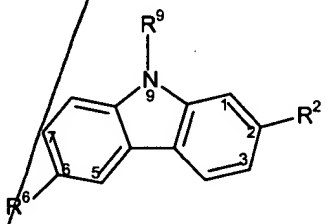
R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, with the proviso that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.

16. (Amended) The method according to claim 15 where the pain and inflammation is caused by osteoarthritis, and administration is once or twice daily by oral administration of a caplet, chewable tablet, or suspension containing from 25 to 100 mg of said drug.

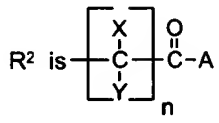
17. (Amended) The method according to claim 15 where the pain and inflammation is caused by osteoarthritis, and administration is once or twice daily by injection containing from 25 to 100 mg of said drug.

18. (Amended) A method of treating a member of the species Canis familiaris, which member has been evaluated and determined to be (1) in need of treatment to alleviate or prevent pain and inflammatory processes and diseases with reduced or no undesirable gastro-intestinal side effects normally associated with administration of non-steroidal anti-inflammatory drugs to said member and (2) said member will benefit by using such treatment from the selective inhibition of inducible cyclo-oxygenase-2 (COX-2) to prevent or alleviate said pain and inflammatory processes with little or reduced inhibition of constitutive cyclo-oxygenase-1 (COX-1) to reduce or avoid said side effects, comprising administering to said member of the species Canis familiaris which has been so evaluated and diagnosed an amount therapeutically effective to treat or prevent pain and inflammation of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, with the proviso that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.

19. (Amended) The method according to claim 18 where the pain and inflammation is caused by osteoarthritis, and administration is once or twice daily by oral administration of a caplet, chewable tablet, or suspension containing from 25 to 100 mg of said drug.

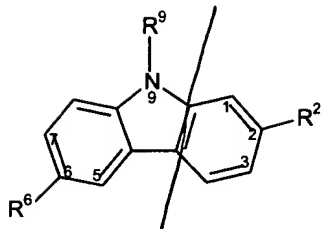
20. (Amended) The method according to claim 18 where the pain and inflammation is caused by osteoarthritis, and administration is once or twice daily by injection containing from 25 to 100 mg of said drug.

21. (Amended) A method of treating a member of the species Canis familiaris to prevent or alleviate pain and inflammatory processes and diseases which comprises administering to a member of such species which has been

a) evaluated and determined by a veterinarian practitioner to be in need of such treatment with a drug which inhibits the activity of inducible cyclo-oxygenase-2(COX-2) to prevent or alleviate said pain and inflammatory processes while

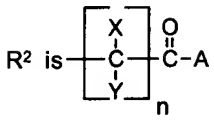
(b) avoiding or reducing the gastro-intestinal side effects normally associated with administration of non-steroidal anti-inflammatory drugs to said member and therefore

(c) to benefit from treatment with a drug that does not substantially inhibit the activity of constitutive cyclo-oxygenase-1(COX-1) so that said side effects are reduced or eliminated, which method comprises administering to said member of the species Canis familiaris which has been so evaluated and determined, a therapeutically effective amount of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation,

whereby such pain and inflammation are prevented or alleviated, said side effects are avoided or reduced and COX-2 is selectively inhibited without substantial inhibition of COX-1, the selective inhibition ratio of COX-2 to COX-1 being at least 3:1 based on ex vivo inhibition levels measured in whole blood, with the proviso that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.

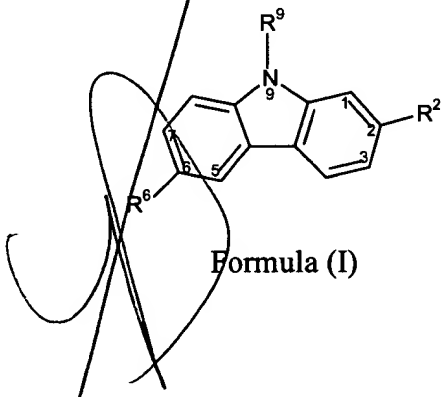
22. (Amended) The method according to claim 21 where the pain and inflammation is caused by osteoarthritis, and administration is once or twice daily by oral administration of a caplet, chewable tablet, or suspension containing from 25 to 100 mg of said drug.

23. (Amended) The method according to claim 21 where the pain and inflammation is caused by osteoarthritis, and administration is once or twice daily by injection containing from 25 to 100 mg of said drug.

24. (Amended) A pharmaceutical combination for treating or preventing pain and inflammatory processes and diseases associated with the activity of inducible cyclo-oxygenase-2 (COX-2) in a member of the species Canis familaris with reduced or no side effects normally associated with the inhibition of the activity of constitutive cyclo-oxygenase -1 (COX-1) comprising

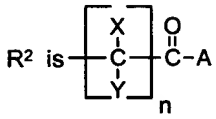
(1) a pharmaceutical composition comprising

(a) a therapeutically effective amount of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, and

(b) a pharmaceutically acceptable carrier therefor, in association with

(2) printed informational material conveying that said pharmaceutical composition contains a therapeutic agent, which when administered to said member effectively inhibits the activity of COX-2 to prevent said pain and inflammatory processes and diseases while reducing or eliminating undesirable gastro-intestinal side effects by substantially avoiding inhibition of the activity of COX-1, with the proviso that said pharmaceutical composition is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.

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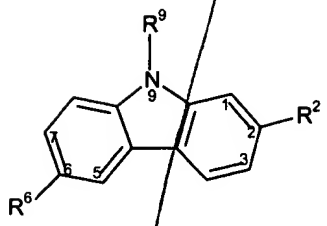
26. (Amended) A method of treating a member of the species Canis familiaris to prevent or alleviate pain and inflammatory processes and diseases which comprises

(a) evaluating said member by a veterinarian practitioner to determine if the member is in need of treatment with a drug which inhibits the activity of inducible cyclo-oxygenase-2 (COX-2),

(b) evaluating said member by a veterinarian practitioner to determine if the member would benefit from the treatment with a drug that does not substantially inhibit the activity of constitutive cyclo-oxygenase-1 (COX-1) so that gastro-intestinal side effects will be reduced or avoided,

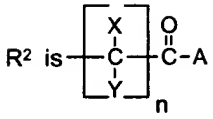
(c) determining that said member will be benefited from the treatment with a drug that selectively inhibits the activity of COX-2 with little or no inhibition of the activity of COX-1, and

(d) administering to said member of the species Canis familiaris which has been so evaluated and determined, a therapeutically effective amount of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation,

whereby such pain and inflammation are prevented or alleviated, said side effects are avoided or reduced and COX-2 is selectively inhibited without substantial inhibition of COX-1, the selective inhibition ratio of COX-2 to COX-1 being at least 3:1 based on ex vivo inhibition levels measured in whole blood, with the proviso that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.

Please add the following new Claims 27-36.

27. A method of treating or preventing pain and inflammatory diseases in a dog comprising administering to a dog in need of such treatment a therapeutically effective amount of a non-racemic mixture of carprofen.